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Rejection of Claims 65 and 66 Under 35 U.S.C. § 112, second paragraph

Claims 65 and 66, which depend from claim 64, have been rejected as because there is insufficient antecedent basis for "said  $\beta$ -secretase protein." Claim 64 has been amended to recite " $\beta$ -secretase protein," thus mooting the rejection. ck

Rejection of Claims 69 Under 35 U.S.C. § 112, second paragraph

Claim 69, which depends from claim 64, has been rejected because there is insufficient antecedent basis for "said  $\beta$ -secretase-cleavable fragments." Claim 64 has been amended depend from claim 67, thus mooting the rejection. ?

Statutory double patenting

Claims 48, 51-62 and 64-69 are provisionally rejected under statutory double patenting as allegedly being unpatentable over claims 56 and 61-77 of copending Application No. 09/501,708. After entry of the amendment filed August 8, 2002 in Application No. 09/501,708, claims 86-90 and 132-141 are under consideration, claims. Thus, Applicants request that the provisional statutory double patenting rejection be withdrawn.

Applicants note that Application Nos. 09/723,722 and 09/724,569 are continuations of Application No. 09/501,708 and, consequently, may have claims that are in conflict of the presently claimed invention.

CONCLUSION

In view of the foregoing, the Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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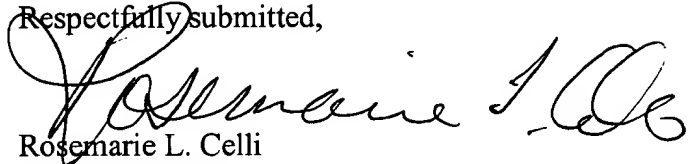
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If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE CLAIMS:**

Please amend the claims as follows.

63. (Amended) The method of claim 58, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2 [[1-501]].

64. (Twice Amended) A heterologous cell, comprising

(i) a nucleic acid molecule encoding a  $\beta$ -secretase protein of SEQ ID NO: 43, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 69, or the complementary sequence of said nucleic acid molecules;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

67. (Amended) The cell of claim 64, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of the wild type  $\beta$ -amyloid precursor protein (APPwt), the Swedish mutant  $\beta$ -amyloid precursor protein (APPsw), and  $\beta$ -secretase cleavable fragments thereof.

68. (Twice Amended) The cell of claim 64, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of  $\beta$ -amyloid precursor protein (APP) having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of  $\beta$ -

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amyloid precursor protein (APP) having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

69. The cell of claim [64]67, wherein said  $\beta$ -secretase-cleavable fragment is selected from the group consisting of SEVKMDAEF (P5-P4'wt), SEVNLDAEF (sw), SEVKLDAEF, SEVKFDAEF, SEVNFDAEF, SEVKMAAEF, SEVNLAAEF, SEVKLAAEF; SEVKMLAEF, SEVNLLAEF, SEVKLLAEF, SEVKFAAEF, SEVNFAAEF, SEVKFLAEF, and SEVNFLAEF.

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